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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,542	03/29/2002	Victor Johannes Nickolson	2000.551US	4736

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,542	NICKOLSON, VICTOR JOHANNES	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2004 and 15 April 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 9-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/10/04, 9/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Summary of Action

1. The rejection of claims 1-3 and 9-17 under 35 USC 103(a) is maintained for the reason of the record.

2. By Amendment filed March 10, 2004, claim 3 has been amended and claims 18 and 19 have been newly added. Claims 1-3, 9-19 are currently pending for the prosecution on the merits.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 1-3 and 9-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lange et al. (DRUGS UNDER EXPERIMENTAL AND CLINICAL RESEARCH, 1995, 21(3), 89-96) in view of Olsen et al. (WO 9819674).

With respect to claims 1-3 and 9-17,

This rejection is analogous to the original rejection.

With respect to claims 18-19,

The newly added claims now require S(+) enantiomer of mirtazapine. However, the individual isomer(s) is obvious variant(s) over the corresponding racemate because of their presence in the racemate. It would further be expected that one of the isomer(s) would be more active than the other and the racemate would exhibit the combined effects. Thus, the references in combination make obvious the instant claims.

Response to Arguments

5. Applicant's arguments filed March 10, 2004 have been fully considered but they are not persuasive.

In response to the rejection of the claims under 35 USC 103(a), the applicants state:

> Olsen '674 discloses on page 32, lines 7-13 that mirtazapine "may also have an effect on glutamine neurotransmission, potentially as non-competitive NMDA receptor antagonists. It is through this mechanism that [mirtazapine is] presumed to provide a method of treatment of tension-type headaches." The only demonstrated anti-headache effects in Olsen '674 are with L-NMMA (page 74-75), Gabapentin (page 91) and Dextromethorphan (page 93). Olsen '674 provides no mechanistic or structural relation between the exemplified drugs and mirtazapine.
>
> Olsen '674 fails to provide any data to support its assertion; therefore, Olsen '674 is merely speculating as to the action of mirtazapine and many other compounds. For example as to the speculation within Olsen '674, Applicant directs the Examiner to speculative claim 14 where Olsen '674 appears recite every possible mechanistic relationship without any support. More importantly, Olsen '674 fails to disclose any combination composition for treatment of headaches containing mirtazapine and a NSAID.

This argument is not persuasive at all. Unlike applicants' allegation, Olsen teaches the use of mirtazapine as NMDA antagonist (functional equivalent of MK-801, desipramine, amitriptylline, imipramine and venlafaxine) that is useful for the treatment of tension type headache. There is no absolute requirement for the inventor to show every working examples in the specification. Thus, reading the whole context of the reference, the skill artisan would have recognized the potential utility of mirtazapine in the treatment of tension type headache (this notion is succinctly elucidated in numerous articles, see "treatment of chronic tension-type headache with mirtazapine", Kulaksizoglu et al., abstract, Frontiers in Headache Research, 2004, 12, 134-137; "Treatment of Chronic Tension Type Headache with Mirtazapine and Amitriptyline", Martin-Araguz et al., abstract, Revista De Neurologia, 2003, 37 (2), 101-5).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Clearly, cited prior art references in combination make that non-steroidal anti-inflammatory drug (e.g., ibuprofen, ketoprofen, naproxen) have been individually used for the treatment of headache, namely tension headache. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).*

Conclusion

6. Applicant's amendment necessitates a new ground of rejection(s) in this Office Action. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

VICKIE KIM
PRIMARY EXAMINER

Brian Kwon
Patent Examiner
AU 1614